IN THE UNITED STATES DISTRICT COURT
DISTRICT OF DELAWARE

NIPPON SHINYAKU CO., LTD., Plaintiff, v. SAREPTA THERAPEUTICS, INC., Defendant.	)	C.A. No. 21-1015 (GBW)
SAREPTA THERAPEUTICS, INC., Defendant and Counter-Plaintiff v. NIPPON SHINYAKU CO., LTD. and NS PHARMA, INC., Plaintiff and Counter-Defendants.	)	[redacted]

LETTER TO THE HONORABLE GREGORY B. WILLIAMS FROM NIPPON SHINYAKU CO. AND NS PHARMA, INC. REGARDING SAREPTA'S MOTION FOR LEAVE TO FILE A SECOND AMENDED ANSWER

Amanda S. Williamson (admitted *pro hac vice*)
Christopher J. Betti (admitted *pro hac* vice)
Krista V. Venegas (admitted *pro hac* vice)
Wan-Shon Lo (admitted *pro hac vice*)
Maria E. Doukas (admitted *pro hac vice*)
Zachary Miller (admitted *pro hac vice*)
Guylaine Haché (admitted *pro hac vice*)
Michael T. Sikora (admitted *pro hac vice*)
Morgan, Lewis & Bockius LLP
110 N. Wacker Drive, Ste 2800
Chicago, IL 60601
Telephone: 312.324.1000
amanda.williamson@morganlewis.com
christopher.betti@morganlewis.com
krista.venegas@morganlewis.com
shon.lo@morganlewis.com
maria.doukas@morganlewis.com
zachary.miller@morganlewis.com
guylaine.hache@morganlewis.com
michael.sikora@morganlewis.com

Amy M. Dudash (DE Bar No. 5741)
Morgan, Lewis & Bockius LLP
1201 N. Market Street, Suite 2201
Wilmington, DE 19801
Telephone: 302.574.3000
amy.dudash@morganlewis.com

Eric Kraeutler (admitted *pro hac vice*)
Alison Patitucci (admitted *pro hac vice*)
Morgan, Lewis & Bockius LLP
1701 Market Street
Philadelphia, PA 19103
Telephone: 215.693.5000
eric.kraeutler@morganlewis.com
alison.patitucci@morganlewis.com

Attorneys for Plaintiff/Counterclaim Defendant Nippon Shinyaku Co., Ltd. and Counterclaim Defendant NS Pharma, Inc.

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Dear Judge Williams:

Nippon Shinyaku ("NS") respectfully opposes the request by Sarepta for leave to amend its answer to add inequitable conduct allegations against the NS patents. First, this Court should deny the motion under Rule 16 because it is untimely and Sarepta cannot demonstrate good cause due to its lack of diligence in seeking amendment. The deadline for amending pleadings was March 23, 2023, and, contrary to Sarepta's assertions, it possessed the key facts underlying its new defenses and counterclaims for months—and, in some cases, years—before that deadline. Second, this Court could also deny Sarepta's motion because its proposed amendments are futile.

I. Sarepta's Motion Should Be Denied Under Rule 16 Because it is Untimely

The deadline for amending pleadings in this case was ***March 23, 2023***. Sarepta did not move to amend its pleadings by that deadline. In fact, Sarepta did not even approach NS with its proposed amendment until nearly four months after the deadline.

When, as here, a party seeks to amend a pleading after the deadline set forth in a scheduling order, that party must satisfy Rule 16. *See, e.g.*, *Truinject Corp. v. Galderma, S.A.*, 2021 WL 4355570, at *2 (D. Del. Sept. 24, 2021). Under Rule 16, "a scheduling order may only be modified for good cause." *Id.* Good cause exists "when the schedule cannot be met despite the moving party's diligence." *iCeutica Pty Ltd. v. Novitium Pharma LLC*, 2019 WL 4604029, at *1 (D. Del. Sept. 23, 2019). Thus, "the good cause standard under Rule 16 hinges on diligence of the movant." *Genentech, Inc. v. Amgen Inc.*, 2020 WL 708113, at *1 (D. Del. Feb 12, 2020). Good cause does not exist "when a party was aware of the facts that would lead it to amend and failed to act on [them]." *Glaxosmithkline LLC v. Glenmark Pharms. Inc.*, 2016 WL 7319670, at *1 (D. Del. Dec. 15, 2016).

Here, Sarepta attempts to justify its failure to comply with this Court's deadline by asserting that it could not have amended its pleadings before March 23 because "NS did not make Mr. Watanabe available for deposition until June 26-27, 2023" and "NS did not produce documents disclosing critical omitted information until June 21, 2023." D.I. 273 at 2. Not so. In fact, as described below, the proposed amended pleading itself reveals that the key facts underlying Sarepta's new inequitable conduct allegations have been in Sarepta's possession for months.

This is particularly well-illustrated with respect to Sarepta's assertion of inequitable conduct based on the allegations that Mr. Watanabe and Mr. Feng misled the USPTO by making [redacted] while purportedly "[redacted]." D.I. 272-2 ¶ 226. For these allegations, Sarepta relies on the prosecution history of the NS Patents (*id.* ¶¶ 126-140), the prosecution history of NS's European Patent No. EP3018211 (*id.* ¶¶ 141-156), the prosecution history of NS's Japanese Patent No. JP6193343 (*id.* ¶¶ 157-159), and NS's Opposition to UWA's European Patent No. EP2206781 (*id.* ¶¶ 160-172). Each of these prosecution histories were ***publicly available to Sarepta since well before this case was filed***, and NS further produced certified prosecution file wrappers for the NS Patents on ***April 18, 2022***.

Sarepta also relies on [redacted] and other NS documents, ***produced on January 20 or February 28, 2023*** (*id.* ¶¶ 190-204), to allege that "[redacted]." *Id.* ¶ 203. Sarepta further relies on a [redacted]

[redacted], ***produced on April 28, 2023*** (*id.* ¶¶ 205-208), to allege that [redacted]." *Id.* ¶ 208.

Tellingly, the ***sole document*** relied upon by Sarepta to support its new inequitable conduct allegations that was produced on June 21, 2023 (the date Sarepta depends on to evidence its motion's purported timeliness), is [redacted] *Id.* ¶¶ 209-213. Sarepta does not even attempt to allege that any of the [redacted] is material to the patentability of the NS Patents. Rather, Sarepta merely relies on it to argue that it allegedly "***further*** supports an intent to deceive the USPTO," *i.e.*, cumulative evidence of a fact Sarepta contends is established by other evidence. D.I. 273 at 1 (emphasis added).

As to Sarepta's assertion of inequitable conduct based on the allegation that "[redacted]" (D.I. 272-2 ¶ 230), Sarepta relies on a document ***produced on May 19, 2023*** (*id.* ¶183) to argue that "[redacted]." *Id.* ¶ 186.[1]

As is clear, the key facts that form the basis of Sarepta's assertion of inequitable conduct ***have been in Sarepta's possession for months***, and well before it filed its motion for leave to amend its answer to add inequitable conduct allegations against the NS patents.

Sarepta also asserts, generally, that it could not have pled its new defenses and counterclaims before the deadline because it relies on [redacted] June 26-27, 2023. But this does not excuse Sarepta's failure to timely amend its pleading. The cited deposition testimony merely corroborated the documentary evidence already in Sarepta's possession. Where, as here, Sarepta already had documentary evidence for all the key facts underlying its allegations, there is no rule requiring it to await confirmatory deposition testimony. *See Chemours Co. FC, LLC v. Daikin Indus., Ltd.*, 2022 WL 855518, at *2 (D. Del. Mar. 23, 2022) (rejecting argument that the heightened pleading requirements for inequitable conduct means "that a party can never file a plausible Rule 9(b)-related claim in a patent case before depositions occur. That is certainly not the rule."). And none of the cases cited by Sarepta are to the contrary. *BigBand Networks, Inc. v. Imagine Commn's, Inc.*, 2010 WL 2898286, at *2 (D. Del. Jul. 20, 2010) (allowing amendment after the deadline because "most of the amendments [defendant] proposes are based upon information gained through depositions after the deadline for amended pleadings expired"); *Intervet Inc., Boehringer Ingelheim Vetmedica, Inc.*, 2012 WL 4808427, at *1 (D. Del. Oct. 9, 2012) (allowing amendment because "key evidence" relied on for the amended pleading was produced after the deadline). Here, in contrast, the facts underlying Sarepta's claims ***have been in Sarepta's possession for months***.

Finally, although Sarepta asserts that inequitable conduct claims are routinely added after the deadline for amended pleadings, where a movant fails to show that it could not have pled the claim prior to the deadline, motions to add inequitable conduct claims after the deadline are

[1] At least one document ***produced by NS on January 20, 2023*** discloses the same information. Exhibit C at NS00062383 (ppt slide disclosing data from "[redacted]).

routinely ***denied***. *See, e.g.*, *Genentech*, 2020 WL 708113, *1 (denying leave to file an amended answer to assert an inequitable conduct defense since the accused infringer sought leave after the scheduling order deadline had passed and unduly delayed by waiting three months after it had sufficient information on the defense to file its motion seeking leave); *Carrier Corp. v. Goodman Glob., Inc.*, 49 F. Supp. 3d 430, 433-34 (D. Del. 2014) (finding that no good cause existed to amend to introduce inequitable conduct when defendant relied on documents produced nearly seven months prior to its motion for leave to amend); *Sonos, Inc. v. D&M Holdings Inc.*, 2017 WL 476279, at *2 (D. Del. Feb. 3, 2017) (denying motion where "[t]he inequitable conduct allegations . . . rest entirely on information that was publicly available months or even years before the deadline for amendments"); *Asahi Glass Co. Ltd. v. Guardian Indus. Corp.*, 276 F.R.D. 417, 420 (D. Del. 2011) (denying motion where "the critical documents to defendant's new inequitable conduct claims" were available before the amendment deadline as part of "the publicly available file wrappers").

II. Sarepta's Allegations of Inequitable Conduct in its Amended Answer Are Futile

A. Sarepta failed to adequately plead that the omitted experimental data was material

Sarepta's allegations must make an initial showing from which it can be reasonably inferred that "but-for" NS's alleged misrepresentations, the USPTO would have not allowed the '361 patent to issue. *See, e.g.*, *Wyeth Holdings Corp. v. Sandoz Inc.*, 2012 WL 600715, at *5-6 (D. Del. Feb. 3, 2012). Although Sarepta's proposed pleading alleges, conclusorily, that "[i]f the USPTO had been aware of [redacted], it would not have allowed the '361 patent" (D.I. 272-2 ¶ 217), Sarepta provides no factual support underlying this barebones but-for materiality allegation. Indeed, Sarepta points to ***nothing*** in the Notice of Allowance indicating that the Examiner relied on NS's evidence of unexpected results in allowing the claims.

To the contrary, the prosecution history belies Sarepta's assertion. While prosecuting the '361 Patent, NS first made the superiority arguments in a Response (July 22, 2016) to the Examiner's Non-Final Office Action rejecting the pending claims as obvious over certain prior art. D.I. 272, Exhibit AI at NS00000761 ("Applicants submit that this superiority is unexpected. . . ."). The Examiner did not find these arguments persuasive, and issued a Final Rejection that again rejected the pending claims as obvious over the same prior art. *Id.* at 775. Importantly, the Examiner expressly noted his disagreement with the superiority argument. *Id.* at 780 ("Applicant asserts that the instant compounds have unexpected properties. The examiner disagrees.").

Subsequent prosecution demonstrates that the Examiner allowed the claims, at least primarily, based on, NS's amendment removing SEQ ID NO: 11 from the claims and limiting them to a sequence consisting of SEQ ID NO: 57. Specifically, in the response preceding the Notice of Allowance, NS amended the claims as follows:

> Claim 1. (Currently Amended): An antisense oligomer which causes skipping of the 53rd exon in the human dystrophin gene, consisting of the nucleotide sequence of ~~SEQ ID NO: 11 or~~ SEQ ID NO: 57 . . .

D.I. 272, Exhibit AI at NS00000788. In the remarks, NS noted that the "amendment is necessary and was not earlier presented because it is made in response to arguments raised in the final rejection." *Id.* at NS00000790. Sarepta's proposed amended pleadings fails to acknowledge that

by deleting SEQ ID NO. 11 (which targets positions 32-56 of exon 53), the claims no longer covered an antisense oligonucleotide that fell "squarely within" the scope of "the oligomer corresponding to positions 30-59 of exon 53 [*e.g.*, Popplewell's PMO-G, which] provides the highest activity," and which the Examiner noted evidenced "a 'superior' target region" of exon 53. *Id.* at NS00000782. NS explained that "[i]n contrast, the presently recited SEQ ID NO: 57 corresponds to positions 36-60. Thus, Popplewell's top performer is different from the presently recited ones." *Id.* at NS00000793.

In view of this amendment, made in the response immediately preceding allowance of the claims, it is not plausible that the Examiner allowed the claims solely based on ("but-for") the allegedly misleading experimental data. As noted, the Examiner had already rejected NS's unexpected results evidence, stating in the Final Office Action that he disagreed with NS's argument that the claimed sequences exhibited unexpected properties. *Id.* at NS00000782 ("***Applicant asserts that the instant compounds have unexpected properties. The examiner disagrees***.") (emphasis added). Nothing in the Examiner's later Notice of Allowance indicates that he had changed his position as to the unexpected results or relied upon them in allowing the claims. *Id.* at NS00000803-807.

B. Sarepta failed to adequately plead that Sazani was material

NS's "failure to submit the Sazani paper" allegation (D.I. 273 at 2) fairs no better. First, Sarepta failed to plausibly allege that Sazani was even material, by showing that it was not cumulative of the cited prior art. To succeed in pleading inequitable conduct, the pleading must explain not only how "the withheld references are material" but also how they are "not cumulative to the information already of record." *Exergen Corp. v. Wal-Mart Stores, Inc.*, 575 F.3d 1312, 1329 (Fed. Cir. 2009). Here, US 2010/0130591 ("'591 Sazani")—which was relied upon by the Examiner during prosecution of the '361 patent (*see* D.I. 272, Exhibit AI at NS00000775)—discloses modifying an antisense oligonucleotide at the 5' end with triethylene glycol. Exhibit A ¶ [0046] ("In yet further embodiments, the moiety that enhances solubility of the oligomer in aqueous medium is triethylene glycol [which] may be conjugated to the oligomer at the 5' end of the oligomer."). It also discloses AVI-4658 as SEQ ID NO: 588. *Id.* ¶ [0299]. And Figure 1A of '591 Sazani "shows an exemplary morpholino oligomer structure with a phosphorodiamidate linkage," *e.g.*, a "PMO." *Id.* at Figure 1A. There is no material difference (***and Sarepta identifies none***) between the triethylene glycol 5' end moiety, the AVI-4658 sequence or the PMO structure disclosed in '591 Sazani and the Sazani paper.

As to the Sazani paper purportedly "establishing, for the first time, the favorable safety profile of an antisense PMO" (D.I. 273 at 2)[2], US 2010/0168212 ("'212 Popplewell")—which was also considered and relied upon by the Examiner during prosecution (D.I. 272, Exhibit AI at NS00000775)—states that "[t]he advantage of a PMO is that it has excellent safety profiles." Exhibit B ¶ [0030]. The Examiner relied on paragraph 30 of '212 Popplewell in rejecting the claims during prosecution. D.I. 272, Exhibit AI at NS00000776-777. And while the Sazani paper additionally discloses genotoxicity testing of AVI-4658, Sarepta does not explain how genotoxicity is in any way relevant to any of the claimed features of the NS Patents. *Telebrands*

[2] *See also* D.I. 272-2 ¶ 228 ("[redacted]").

Corp. v. 1byOne Prod., Inc., 2018 WL 3696558, at *3 (D. Del. Aug. 3, 2018) ("The pleading also fails to address the 'how' factor, offering no explanation as to how a reasonable examiner would use the omitted prior art references in determining the patentability of the Asserted Patents."); *Exergen Corp.*, 575 F.3d at 1329 (finding that the pleading did not sufficiently identify the "what" because it did not disclose specific claim language or claim numbers to establish the materiality of the omitted prior art references to the patents-in-suit). In short, Sarepta has failed to adequately plead that Sazani was but-for material and should have been disclosed to the USPTO.

Sarepta also fails to plead that [redacted] the USPTO. Sarepta merely alleges that "[redacted]." D.I. 272-2 ¶ 228. But knowledge alone does not rise to the level of demonstrating specific intent. *1st Media, LLC v. Elec. Arts, Inc.*, 694 F.3d 1367, 1374 (Fed. Cir. 2012) ("Knowledge of the reference and knowledge of materiality alone are insufficient after *Therasense* to show an intent to deceive."). Regardless, that the Sazani paper's "[redacted]" (D.I. 272-2 ¶ 183) does not establish the materiality of the Sazani paper ***to the NS Patents***.

C. Sarepta Failed to Adequately Plead Infection of the Continuation Family Members

Sarepta failed to plead the existence of an "immediate and necessary relation" between the continuation patents and the purported inequitable conduct committed during prosecution of the '361 patent. *Consol. Aluminum Corp. v. Foseco Int'l, Ltd.*, 910 F.2d 804, 810-11 (Fed. Cir. 1990). The only allegations are found in the proposed amended pleading at paragraph 218 which summarily states that "[t]he materiality of the misrepresentation and [redacted] equally applies to each of the '092, '461, '106, '741, '217, and '322 patents" because "each of the … patents is directed to substantially the same subject matter as the '361 patent" and the examiner allowed "each of the . . . patents without any prior art rejection under 35 U.S.C. § 102 or § 103."

"[U]nenforceability of a parent patent for inequitable conduct does not automatically render the later-issued descendants of that patent unenforceable." *Abbott Labs. v. Sandoz Inc.*, 500 F. Supp. 2d 807, 819 (N.D. Ill. 2007). A party pleading infection of subsequently issued patents must "allege an immediate and necessary relation between the [infected] patent and the specific inequitable conduct alleged[;]" a showing of a "substantial relationship" is not enough. *Bone Care Int'l, LLC v. Pentech Pharm., Inc.*, 2010 WL 1655455, at *3 (N.D. Ill. Apr. 23, 2010) (granting motion to dismiss inequitable conduct defense where defendant pleaded only a "substantial relationship" between the patents); *Power Integrations, Inc. v. Fairchild Semiconductor Int'l, Inc.*, 2009 WL 4928024, at *9 (D. Del. Dec. 18, 2009) report and recommendation adopted, 2010 WL 2990039 (D. Del. July 22, 2010) (granting motion to dismiss infectious unenforceability defense because the defendant failed to plead sufficient facts to "establish the required 'immediate and necessary relation.'") (quoting *Consol. Aluminum*, 910 F.2d at 810-11). The mere fact that the '361 patent and the asserted continuations are "directed to substantially the same subject matter" "is not sufficient to invoke the infectious unenforceability doctrine." *Abbott Labs*, 500 F. Supp. 2d at 819; *Bone Care*, 2010 WL 1655455, at *3; *Power Integrations*, 2009 WL 4928024, at *9.

For the foregoing reasons, NS respectfully requests that the Court deny Sarepta's motion without leave to amend.

July 26, 2023

Respectfully submitted,

MORGAN, LEWIS & BOCKIUS LLP

/s/Amy M. Dudash

Amy M. Dudash (DE Bar No. 5741)
1201 N. Market Street, Suite 2201
Wilmington, Delaware 19801
Telephone: 302.574.3000
Fax: 302.574.3001
amy.dudash@morganlewis.com

Attorneys for Plaintiff/Counterclaim Defendant Nippon Shinyaku Co., Ltd. and Counterclaim Defendant NS Pharma, Inc.

Amanda S. Williamson (admitted *pro hac vice*)
Christopher J. Betti (admitted *pro hac* vice)
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Zachary Miller (admitted *pro hac vice*)
Guylaine Haché (admitted *pro hac vice*)
Michael T. Sikora (admitted *pro hac vice*)
110 N. Wacker Drive, Ste 2800
Chicago, IL 60601
Telephone: 312.324.1000
Fax: 312.324.1001
amanda.williamson@morganlewis.com
christopher.betti@morganlewis.com
krista.venegas@morganlewis.com
shon.lo@morganlewis.com
maria.doukas@morganlewis.com
zachary.miller@morganlewis.com
guylaine.hache@morganlewis.com
michael.sikora@morganlewis.com

Eric Kraeutler (admitted *pro hac vice*)
Alison Patitucci (admitted *pro hac vice*)
1701 Market Street
Philadelphia, PA 19103
Telephone: 215.693.5000
Fax: 215.963.5001
eric.kraeutler@morganlewis.com
alison.patitucci@morganlewis.com